Amendments to the Specification:

Please replace paragraph beginning at line 18 of page 7 with the following amended paragraph:

Herein, the phrase "complementary to a nucleotide sequence" encompasses not only cases wherein a nucleotide sequence completely pairs with the template, but also includes those that have at least 70%, preferably 80%, more preferably 90%, and even more preferably 95% or more (for example, 97% or 99%) of the nucleotides paired with the template. To pair refers to the formation of a chain, in which T (U in the case of an RNA) corresponds to A, A corresponds to T or U, G corresponds to C, and C corresponds to G in the nucleotide sequence of the template polynucleotide. Homologies at the nucleotide sequence level between certain polynucleotides can be determined by the BLAST algorithm (Altschul (1990) Proc. Natl. Acad. Sci. USA 87: 2264-8; Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90: 5873-7). The BLASTN program for nucleotide sequences (Altschul *et al.* (1990) J. Mol. Biol. 215: 403-410) has been developed based on this algorithm, and can be used to determine the homology of marker polynucleotide probe sequences ~~(see http://www.ncbi.nlm.nih.gov for a specific example of analysis methods)~~.

Please replace paragraph beginning at line 8 of page 9 with the following amended paragraph:

References such as Molecular Cloning, A Laboratory Manual 2nd ed. (Cold Spring Harbor Press (1989); Section 9.47-9.58), Current Protocols in Molecular Biology (John Wiley & Sons (1987-1997); Section 6.3-6.4), DNA Cloning 1: Core Techniques, A Practical Approach 2nd ed. (Oxford University (1995); Section2.10 for conditions, in particular), can be referred to for detailed information on hybridization procedures. Examples of hybridizing polynucleotides include polynucleotides containing a nucleotide sequence that has at least 50% or more, preferably 70%, more preferably 80% and even more preferably 90% (for example, 95% or more, or 99%) identity with a nucleotide sequence comprising the nucleotides of SEQ ID NO: 1 or SEQ ID NO: 2. Such identities can be determined by the BLAST algorithm (Altschul (1990) Proc. Natl. Acad. Sci. USA 87: 2264-8; Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90: 5873-7) as described in the homology determination above. In addition to the above-

described BLASTN program for nucleotide sequences, the BLASTX program for determining the identity of amino acid sequences (Altschul *et al.* (1990) J. Mol. Biol. 215: 403-10) and the like have been developed based on this algorithm and can be used ~~(as described above, see http://www.ncbi.nlm.nih.gov. for a specific example of analysis methods)~~.

Please replace paragraph beginning at line 36 of page 24 with the following amended paragraph:

Gene expression regulatory regions can be predicted using a program such as Neural Network (~~http://www.fruitfly.org./seq_tools/promoter.html;~~ Reese *et al.*, Biocomputing: Proceedings of the 1996 Pacific Symposium, Hunter and Klein ed., World Scientific Publishing Co., Singapore, (1996)). Moreover, a program for predicting the minimum unit required for the activity of an expression regulatory region is also known, (~~http://biosci.cbs.umn.edu./software/proscan/promoterscan. htm;~~ Prestridge (1995) J. Mol. Biol. 249: 923-932), and can be used.

Please replace paragraph beginning at line 4 of page 28 with the following amended paragraph:

The nucleotide sequence of an siRNA can be designed using a computer program such as that disclosed at the Ambion website ~~(http://www.ambion.com/techlib/misc/siRNA_finder.html)~~. Kits for screening for functional siRNAs are also commercially available and can be used (for example, BD Knockout RNAi System (BD Biosciences Clontech).

Please replace paragraph beginning at line 25 of page 28 with the following amended paragraph:

Fig. 7 **A-D are** ~~is~~ a set of photographs showing the results of Lrp4 mRNA expression analysis in E12.5 mouse central nervous system by *in situ* hybridization. A: sagittal cross-section, B: enlarged photograph of the area inside the box of A, C: cross-section at the location of the red line of A, D: Expression of Lrp4, Shh, and tyrosine hydroxylase (TH) mRNA in E12.5 mouse midbrain ventral region.